Age-associated cognitive decline is related to biological life events

43 Age-Associated Cognitive Decline is Related to Biological Life Events

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Several studies consistently show a decline of cognitive abilities that is associated with aging. Most of this research was directed towards the deterioration of memory functions (1). Up to now, studies have typically been concerned with a group of elderly subjects of about 70 years or older, whose performance was compared with that of younger adults, mostly students. In addition, hardly any attention has been paid to the possibility of brain dysfunction in supposedly normal and healthy volunteers. This approach can have a serious drawback, as old people are more likely to have been exposed to some agent that hampers the optimal functioning of the brain. For these agents the term 'biological life events' (BLE) is proposed here. BLE are factors that are known to damage optimal brain functioning, other than severely impairing conditions such as trauma, psychiatric disease with cognitive disorders, or dementia. As yet, no consensus exists about these factors. Examples of BLE are mild, closed head injuries (2), repeated anaesthesia, or intoxication (3).

The present study investigates the possibility that BLE might interact with aging in its effect on memory. The hypothesis was tested that there is little or no memory decline in successive age groups from 20 to 80 years when no demonstrable BLE has been sustained by any of the volunteers. In addition, it was hypothesized that when one or more BLE can be identified in individuals, their average performance is inferior, and this gap widens between older age groups. This contradicts the prevailing notion that memory impairment is a normal, inevitable concomitant of advancing age (see for instance reference 4).

METHOD

Subjects

Data are presented of 112 subjects, who were assigned to seven distinct age groups with mean ages of 20 to 80 years, centered around whole tens of years (20 ± 2 years, 30 ± 2 years, etc.). Within each group subjects were balanced for sex and level of education. Prior to, as well as during, the actual testing, a very thorough health screening for BLE took place. Subjects had subjectively rated their health by filling in a questionnaire concerning general health and in particular brain functioning (e.g. dementia, severe trauma, closed head injury, intoxication, hypoxia, ischemia).

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Applicants who had sustained anything that is known to hamper optimal brain functioning were excluded. Thus, none of the subjects had an a priori likelihood of brain dysfunctioning. During the examination the subjects were interviewed about BLE by an experienced neurologist who, when in doubt, consulted their medical files. The following BLE were regarded as criteria to assign subjects to a separate BLE group, as opposed to a group of subjects of equal size:

1. present or past treatment by a neurologist for epilepsy, migraine, meningitis, encephalitis, etc.
2. present or past treatment for diseases with possible brain impact (e.g. renal dysfunction or hypertension)
3. more than three closed head injuries, or one with amnesia of more than 1 hour
4. undergoing general anaesthesia more than three times, or one time lasting for more than 3 hours
5. medication affecting driving ability or consciousness
6. heavy drinking—i.e. more than 35 glasses per week (for men) or 21 glasses per week (for women)
7. other neurotoxic factors (e.g. chronic exposure to organic solvents)
8. treatment for psychiatric problems within the last 5 years
9. perinatal complications or developmental problems of early childhood.

Having sustained any of these factors sufficed for the subjects to be assigned to the BLE group. Thus, in each age group there were eight subjects who had sustained BLE, and eight subjects who had not. All subjects were paid for their participation in the experiment.

Neuropsychological tests

Experimental evidence presented here concerns several aspects of memory functioning, along with another well-known test (5):

1. visual and auditory short-term memory: block span and digit span
2. speed of memory scanning and sensomotoric processing: a paper-and-pencil information processing task
3. verbal memory consolidation and retrieval: free-recall verbal learning test with testing of delayed recall and recognition
4. speeded reading, color naming and perceptual interference susceptibility: Stroop test.

Procedure

Health screening and testing were part of a standardized procedure which took about two hours. An extensive neurological examination with special focus on pathological and primitive reflexes took place (6). Apart from the tests mentioned above, several other areas of cognitive functioning were studied (7).

RESULTS

Figure 1 depicts the performance on the memory scanning task. Subjects were requested to memorize a set of 1-4 characters. The time needed to cross out 24 target characters on a test sheet with 120 distractor letters is plotted against the number of different targets that have to be memorized. In this vein, speed of cognitive processing relative to the memory load can be assessed. When the target character is the salient '%' sign, the memory load is negligible. Digits still place little load on the memory, as they can easily be discerned from the distractor letters (8).

Every successive age group needed more time to cross out all '%' signs ($F[6,96] = 10.03$, $P < 0.001$), indicating that perceptual and motor processes were slower in all older subjects. Subdivision based on BLE was not statistically significant ($F[1,96] = 2.79$, $P < 0.1$). Crossing out digits was also slower in all elderly subjects ($F[6,96] = 13.68$, $P < 0.001$). Moreover, BLE-affected subjects needed even more time ($F[1,96] = 8.33$, $P < 0.01$). In addition, the effect of memory load was larger in the elderly ($F[6,96] = 3.06$, $P < 0.001$), and in the BLE group ($F[1,96] = 5.10$, $P < 0.01$). When target characters were letters, and therefore the memory load was greatest, this pattern of results was repeated, only more clearly so. The occurrence of BLE and age even appeared to interact significantly with memory load: with increasing memory set and group age the performance was slower, and slower still if BLE had been sustained.

Test performance on the verbal learning test is graphically summarized in Figure 2. A list of 15 monosyllabic words was administered for five successive learning trials

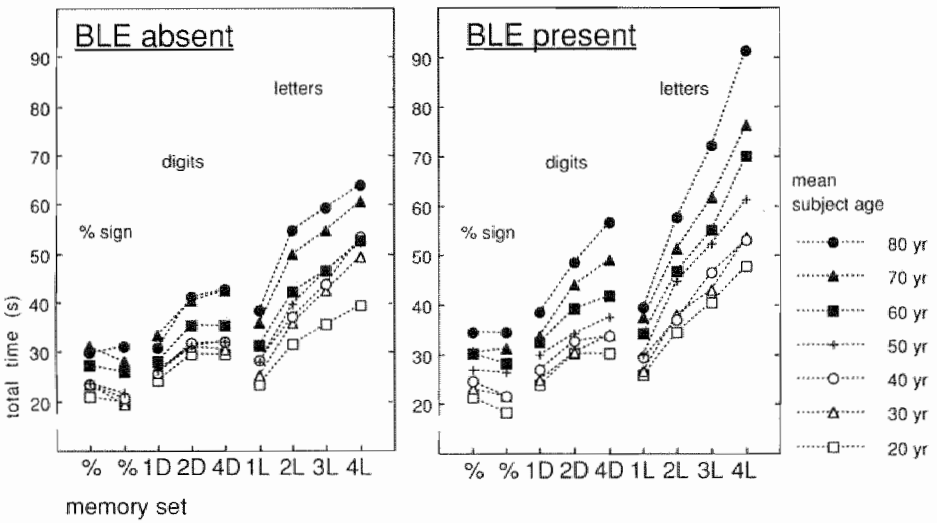

Figure 1. Memory scanning speed. Performance on paper-and-pencil memory scanning task in seven age groups, and in subjects who have (right) or have not (left) sustained biological life events (BLE). The *x*-axis represents the number and nature of different target items to be remembered and subsequently crossed out: % sign (2 trials), 1/2/4 digits, and 1/2/3/4 letters. Each sheet contains 24 targets among 120 distractors

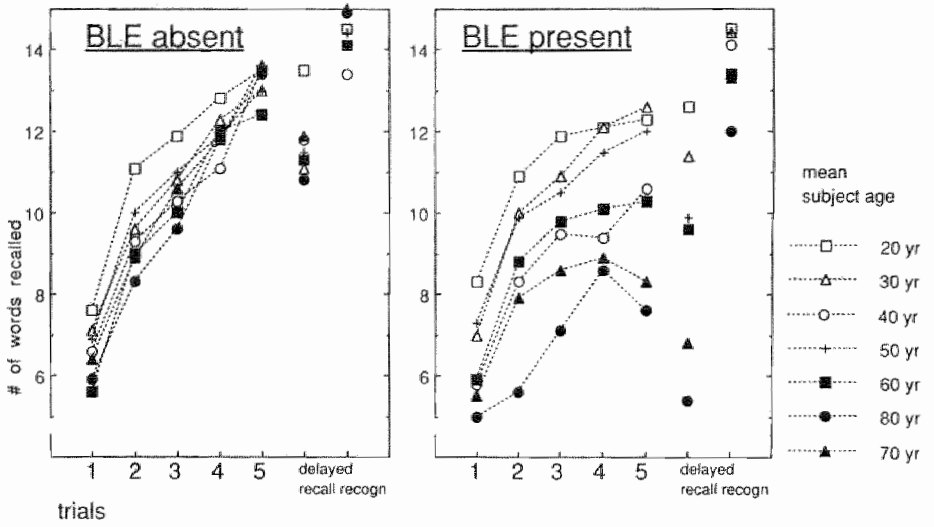

Figure 2. Immediate and delayed repeated free recall of verbal material. Repeated free recall of 15 monosyllabic words, after five repeated presentations in seven age groups, with or without BLE. Not connected by lines are delayed recall and recognition after 20 minutes

at which immediate free recall was tested. Delayed free recall was examined after some 20 minutes, followed by a recognition trial in which the words had to be identified among 15 others.

Subject age significantly affected the performance over all five learning trials ($F[6,98] = 9.87$, $P < 0.001$), as did BLE ($F[1,98] = 24.21$, $P < 0.001$). These effects also interacted ($F[6,98] = 3.16$, $P < 0.01$), indicating that age-related decline of memory performance is further aggravated by BLE. Subjects in the BLE group appeared to profit less from repeated presentation of the words ($F[4,392] = 16.40$, $P < 0.001$). The BLE-unaffected group showed very little age-related decline of the maximal trial score, whereas the elderly BLE subjects did ($F[1,98] = 130.73$, $P < 0.001$), and this effect interacted with age ($F[6,98] = 10.10$, $P < 0.001$), which means that elderly BLE subjects have much less memory capacity than the corresponding BLE-free age groups. Their ability to recall items after 20 minutes was also sharply reduced: $F[1,98] = 155.57$, $P < 0.001$ (main effect); $F[6,98] = 17.93$, $P < 0.001$ (interaction). Delayed recognition was only affected by age if BLE had been sustained: $F[1,98] = 7.13$, $P < 0.01$ (main effect); $F[6,98] = 4.25$, $P < 0.001$ (interaction).

Figure 3 (left) depicts the auditory and visual memory span performance. Analysis showed effects of age group ($F[6,97] = 2.97$, $P < 0.05$) and BLE ($F[1,98] = 4.46$, $P < 0.05$). There was no interaction between these main effects.

Not only memory-related tests showed effects of age or BLE. All factors yielded large and significant main and interaction effects in Stroop performance. Moreover, the susceptibility to perceptual interference proved showed effects of age ($F[6,97] = 11.52$, $P < 0.001$), BLE ($F[1,97] = 22.58$, $P < 0.001$), and a large

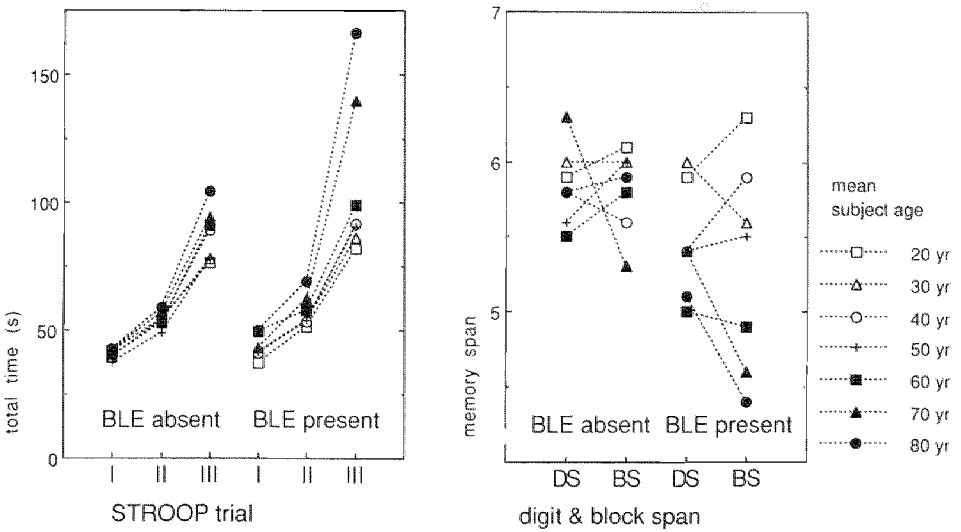

Figure 3. Stroop performance and memory span. Left: performance on three consecutive trials of the Stroop test, involving speeded word reading (I), color naming (II), and colored word reading with language interference. Right: immediate span of auditory and visual memory, as measured by digit span and block span. Both graphs depict seven age groups with either BLE present or absent

interaction effect ($F[6,97] = 4.12$, $P < 0.001$). This suggests that the occurrence of BLE severely aggravates the age-related increase of interference susceptibility.

DISCUSSION

The results show a very small but systematic cross-sectional effect of advancing age in nearly all aspects of memory that were studied in the subjects who were free of biological life events (BLE). The immediate memory span is slightly reduced, the speed and ease of memory search processes (including perceptual and motor processes), verbal memory performance during repeated item presentation, delayed retrieval of newly learned information, and consolidation into memory. An important exception is the maximal performance after repeated presentation. When given time and opportunity to rehearse, healthy elderly people performed almost as well as young subjects. These data are inconsistent with a homogeneous decline in the whole aging population (4). All age-related performance decrements were substantially larger in the BLE age groups. However, this group effect of BLE was already apparent in younger subjects (sometimes as young as 20 or 30 years). The interaction between the effects of age and BLE was not confined to memory functions. Interference susceptibility showed a similar pattern of outcomes, as did several other aspects of cognitive functioning (7). This also implies that health screening is obligatory in experimental research with normal (and therefore supposedly healthy) elderly volunteers.

In elderly BLE-affected subjects, the global cognitive decrement in performance was compatible with the dysfunctions found in incipient dementia. This is best illustrated with the finding of an incomplete memory consolidation, exclusively in the older BLE groups: some of the previously learned items were not even recognized, which is a common finding in dementing patients (1). It is thus proposed that BLE can contribute to the appearance of dementia in the later stages of life. As was stated above, none of the subjects had an a priori likelihood of cognitive dysfunctions due to major brain damage or dementia. The observed group differences are therefore attributable to BLE, instead of any disorder or biological aging. BLE may well be one of the risk factors for incipient dementia. This is consistent with the findings of Amaducci et al (9) who identified a number of risk factors for clinically diagnosed Alzheimer's disease. Presently, a follow-up study is planned with the same subjects. It is hypothesized that the BLE-affected subjects will show more cognitive deterioration and that the incidence of dementia will be highest in the BLE groups.

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